CLAIMS

We claim:

1. A double-stranded ribonucleic acid (dsRNA) for inhibiting the expression of a cellular FLICE-like inhibitory protein (cFLIP) gene in a cell, wherein the dsRNA comprises a complementary RNA strand comprising a nucleotide sequence which is complementary to at least a part of the cFLIP gene.

2. The dsRNA of claim 1, further comprising a sense RNA strand, and wherein at least one end of said dsRNA comprises a nucleotide overhang of 1 to 4 nucleotides in length.

3. The dsRNA of claim 2, wherein the nucleotide overhang is 2 or 3 nucleotides in length.

4. The dsRNA of claim 2, wherein the nucleotide overhang is at the 3'-terminus of the complementary RNA strand.

5. The dsRNA of claim 4, wherein the dsRNA comprises a blunt end, wherein the blunt end is at the 5'-end of the complementary RNA strand.

6. The dsRNA of claim 1, wherein the nucleotide sequence is less than 25 nucleotides in length.

7. The dsRNA of claim 1, wherein the nucleotide sequence is 19 to 24 nucleotides in length.

8. The dsRNA of claim 1, wherein the nucleotide sequence is 20 to 24 nucleotides in length.

9. The dsRNA of claim 1, wherein the nucleotide sequence is 21 to 23 nucleotides in length.

10. The dsRNA of claim 1, wherein the nucleotide sequence is 22 or 23

nucleotides in length.

11. The dsRNA of claim 1, wherein the complementary RNA strand is less than 30 nucleotides in length.

12. The dsRNA of claim 1, wherein the complementary RNA strand is less than 25 nucleotides in length.

13. The dsRNA of claim 1, wherein the complementary RNA strand is 21 to 24 nucleotides in length.

14. The dsRNA of claim 1, wherein the complementary RNA strand is 23 nucleotides in length.

15. The dsRNA of claim 1, wherein the dsRNA further comprises a second (sense) RNA strand.

16. The dsRNA of claim 15, wherein the complementary RNA strand is 23 nucleotides in length and the second RNA strand is 21 nucleotides in length.

17. The dsRNA of claim 16, further comprising a blunt end and a nucleotide overhang of 2 nucleotides in length, wherein the nucleotide overhang is at the 3'-end of the complementary RNA strand and the blunt end is at the 5'-end of the complementary RNA strand.

18. The dsRNA of claim 1, wherein the nucleotide sequence of the complementary RNA strand is complementary to a primary or processed RNA transcript of the cFLIP gene.

19. The dsRNA of claim 15, wherein the complementary RNA strand comprises SEQ ID NO:2 and the second RNA strand comprises SEQ ID NO:1.

20. The dsRNA of claim 15, wherein the complementary RNA strand comprises SEQ ID NO:4 and the second RNA strand comprises SEQ ID NO:3.

21. The dsRNA of claim 15, wherein the complementary RNA strand comprises SEQ ID NO:7 and the second RNA strand comprises SEQ ID NO:1.

22. The dsRNA of claim 15, wherein the complementary RNA strand comprises SEQ ID NO:8 and the second RNA strand comprises SEQ ID NO:3.

23. A method for inhibiting the expression of a cellular FLICE-like inhibitory protein (cFLIP) gene in a cell, the method comprising:

(a) introducing into the cell a double-stranded ribonucleic acid (dsRNA), wherein the dsRNA comprises a complementary RNA strand comprising a nucleotide sequence which is complementary to at least a part of the cFLIP gene; and

(b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of a mRNA transcript of the cFLIP gene, thereby inhibiting expression of the cFLIP gene in the cell.

24. The method of claim 23, further comprising a second (sense) RNA strand.

25. The method of claim 24, wherein at least one end of the dsRNA comprises a nucleotide overhang of 1 to 4 nucleotides in length.

26. The method of claim 25, wherein the nucleotide overhang is 2 or 3 nucleotides in length.

27. The method of claim 25, wherein the nucleotide overhang is at the 3'-terminus of the complementary RNA strand.

28. The method of claim 27, wherein the dsRNA further comprises a blunt end, and wherein the blunt end is at the 5'-end of the complementary RNA strand.

29. The method of claim 23, wherein the nucleotide sequence is less than 25 nucleotides in length.

30. The method of claim 23, wherein the nucleotide sequence is 19 to 24

nucleotides in length.

31. The method of claim 23, wherein the nucleotide sequence is 20 to 24 nucleotides in length.

32. The method of claim 23, wherein the nucleotide sequence is 21 to 23 nucleotides in length.

33. The method of claim 23, wherein the nucleotide sequence is 22 or 23 nucleotides in length.

34. The method of claim 23, wherein the complementary RNA strand is less than 30 nucleotides in length.

35. The method of claim 23, wherein the complementary RNA strand is less than 25 nucleotides in length.

36. The method of claim 23, wherein the complementary RNA strand is 21 to 24 nucleotides in length.

37. The method of claim 23, wherein the complementary RNA strand is 23 nucleotides in length.

38. The method of claim 23, wherein the dsRNA further comprises a second (sense) RNA strand.

39. The method of claim 38, wherein the complementary RNA strand is 23 nucleotides in length and the second RNA strand is 21 nucleotides in length.

40. The method of claim 39, wherein the dsRNA comprises a blunt end and a nucleotide overhang of 2 nucleotides in length, wherein the complementary RNA strand further comprises a 3'-end and a 5'-end, and wherein the nucleotide overhang is at the 3'-end of the complementary RNA strand and the blunt end is at the 5'-end of the complementary RNA strand.

41. The method of claim 23, wherein the nucleotide sequence of the complementary RNA strand is complementary to a primary or processed RNA transcript of the cFLIP gene.

42. The method of claim 24, wherein the complementary RNA strand comprises SEQ ID NO:2 and the second RNA strand comprises SEQ ID NO:1.

43. The method of claim 24, wherein the complementary RNA strand comprises SEQ ID NO:4 and the second RNA strand comprises SEQ ID NO:3.

44. The method of claim 24, wherein the complementary RNA strand comprises SEQ ID NO:7 and the second RNA strand comprises SEQ ID NO:1.

45. The method of claim 24, wherein the complementary RNA strand comprises SEQ ID NO:8 and the second RNA strand comprises SEQ ID NO:3.

46. The method of claim 23, wherein the cell is a tumor cell.

47. The method of claim 46, wherein the tumor cell is resistant to treatment with an apoptosis-inducing drug.

48. The method of claim 47, wherein the apoptosis-inducing drug is TRAIL.

49. A pharmaceutical composition for improving the effectiveness of an apoptosis-inducing drug in a mammal, comprising a dsRNA and a pharmaceutically acceptable carrier, wherein the dsRNA comprises a complementary RNA strand comprising a complementary nucleotide sequence which is complementary to at least a part of a cellular FLICE-like inhibitory protein (cFLIP) gene.

50. The pharmaceutical composition of claim 49, wherein the apoptosis-inducing drug is a tumor necrosis factor (TNF) or a TNF-related ligand.

51. The pharmaceutical composition of claim 50, wherein the TNF-related ligand is selected from the group of ligands consisting of a TRAMP ligand, a CD95 ligand, a TNFR-1 ligand, and a TNF-related apoptosis-inducing ligand (TRAIL).

52. The pharmaceutical composition of claim 50, wherein the TFN-related ligand is TRAIL.

53. The pharmaceutical composition of claim 49, wherein the dsRNA further comprises a nucleotide overhang of 1 to 4 nucleotides in length.

54. The pharmaceutical composition of claim 53, wherein the nucleotide overhang is at the 3'-terminus of the complementary RNA strand.

55. The pharmaceutical composition of claim 49, wherein the nucleotide sequence is less than 25 nucleotides in length.

56. The pharmaceutical composition of claim 49, wherein the nucleotide sequence is 19 to 24 nucleotides in length.

57. The pharmaceutical composition of claim 49, wherein the nucleotide sequence is 20 to 24 nucleotides in length.

58. The pharmaceutical composition of claim 49, wherein the nucleotide sequence is 21 to 23 nucleotides in length.

59. The pharmaceutical composition of claim 49, wherein the nucleotide sequence is 22 or 23 nucleotides in length.

60. The pharmaceutical composition of claim 49, wherein the complementary RNA strand is less than 30 nucleotides in length.

61. The pharmaceutical composition of claim 49, wherein the complementary RNA strand is less than 25 nucleotides in length.

62. The pharmaceutical composition of claim 49, wherein the complementary RNA strand is 21 to 24 nucleotides in length.

63. The pharmaceutical composition of claim 49, wherein the complementary RNA strand is 23 nucleotides in length.

64. The pharmaceutical composition of claim 49, wherein the dsRNA further comprises a second (sense) RNA strand.

65. The pharmaceutical composition of claim 64, wherein the complementary RNA strand is 23 nucleotides in length and the second RNA strand is 21 nucleotides in length.

66. The pharmaceutical composition of claim 65, wherein the dsRNA comprises a blunt end and a nucleotide overhang of 2 nucleotides in length, wherein the complementary RNA strand comprises a 3'-end and a 5'-end, and wherein the nucleotide overhang is at the 5'-end of the complementary RNA strand and the blunt end is at the 3'-end of the complementary RNA strand.

67. The pharmaceutical composition of claim 49, wherein the nucleotide sequence of the complementary RNA strand is complementary to a primary or processed RNA transcript of the cFLIP gene.

68. The pharmaceutical composition of claim 64, wherein the complementary RNA strand comprises SEQ ID NO:2 and the second RNA strand comprises SEQ ID NO:1.

69. The pharmaceutical composition of claim 64, wherein the complementary RNA strand comprises SEQ ID NO:4 and the second RNA strand comprises SEQ ID NO:3.

70. The pharmaceutical composition of claim 64, wherein the complementary RNA strand comprises SEQ ID NO:7 and the second RNA strand comprises SEQ ID NO:1.

71. The pharmaceutical composition of claim 64, wherein the complementary RNA strand comprises SEQ ID NO:8 and the second RNA strand comprises SEQ ID NO:3.

72. The pharmaceutical composition of claim 49, wherein the mammal is a

human.

73. The pharmaceutical composition of claim 49, wherein the dosage unit of dsRNA is less than 5 milligram of dsRNA per kilogram body weight of the mammal.

74. The pharmaceutical composition of claim 49, wherein the dosage unit of dsRNA is in a range of 0.01 to 2.5 milligrams, 0.1 to 200 micrograms, or 0.1 to 100 micrograms per kilogram body weight of the mammal.

75. The pharmaceutical composition of claim 49, wherein the dosage unit of dsRNA is less than 50 micrograms of dsRNA per kilogram body weight of the mammal.

76. The pharmaceutical composition of claim 49, wherein the dosage unit of dsRNA is less than 25 micrograms per kilogram body weight of the mammal.

77. The pharmaceutical composition of claim 49, wherein the pharmaceutically acceptable carrier is an aqueous solution.

78. The pharmaceutical composition of claim 77, wherein the aqueous solution is phosphate buffered saline.

79. The pharmaceutical composition of claim 49, wherein the pharmaceutically acceptable carrier comprises a micellar structure selected from the group consisting of a liposome, capsid, capsoid, polymeric nanocapsule, and polymeric microcapsule.

80. The pharmaceutical composition of claim 79, wherein the micellar structure is a liposome.

81. The pharmaceutical composition of claim 49, wherein the pharmaceutical composition is formulated for administration by inhalation, oral ingestion, infusion or injection.

82. The pharmaceutical composition of claim 49, wherein the composition is formulated for administration by intravenous, intraparenteral, or intratumoral infusion or

injection.

83. A method for improving the effectiveness of a bioactive substance that induces receptor-mediated apoptosis in a tumor cell in a mammal, which comprises administering to said mammal a pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) and a pharmaceutically acceptable carrier, wherein the dsRNA comprises a complementary RNA strand comprising a complementary nucleotide sequence which is complementary to at least a part of a cellular FLICE-like inhibitory protein (cFLIP) gene.

84. The method of claim 83, wherein the bioactive substance is a tumor necrosis factor (TNF) or a TNF-related ligand.

85. The method of claim 84, wherein the TNF-related ligand is selected from the group of ligands consisting of a TRAMP ligand, a CD95 ligand, a TNFR-1 ligand, and a TNF-related apoptosis-inducing ligand (TRAIL).

86. The method of claim 84, wherein the TNF-related ligand is TRAIL.

87. A method for treating cancer in a mammal, the method comprising:

a) administering to the mammal a pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA), wherein the dsRNA comprises a complementary RNA strand comprising a nucleotide sequence which is complementary to at least a part of a cellular FLICE-like inhibitory protein (cFLIP) gene; and

(b) administering to the mammal a pharmaceutical composition comprising a bioactive substance that induces receptor-mediated apoptosis in a tumor cell.

88. The method of claim 87, wherein the bioactive substance is a tumor necrosis factor (TNF) or a TNF-related ligand.

89. The method of claim 88, wherein the TNF-related ligand is selected from the group of ligands consisting of a TRAMP ligand, a CD95 ligand, a TNFR-1 ligand,

and a TNF-related apoptosis-inducing ligand (TRAIL).

90. The method of claim 88, wherein the TNF-related ligand is TRAIL.

91. The method of claim 87, wherein the dsRNA and the bioactive substance are administered together in one pharmaceutical composition.

92. A pharmaceutical composition for inhibiting the expression of a cellular FLICE-like inhibitory protein (cFLIP) in a mammal, comprising a dsRNA and a pharmaceutically acceptable carrier, wherein the dsRNA comprises a complementary RNA strand comprising a complementary nucleotide sequence which is complementary to at least a part of the cFLIP gene.

93. The pharmaceutical composition of claim 92, further comprising an apoptosis-inducing drug.

94. The pharmaceutical composition of claim 93, wherein the apoptosis-inducing drug is a tumor necrosis factor (TNF) or a TNF-related ligand.

95. The pharmaceutical composition of claim 94, wherein the TNF-related ligand is selected from the group of ligands consisting of a TRAMP ligand, a CD95 ligand, a TNFR-1 ligand, and a TNF-related apoptosis-inducing ligand (TRAIL).

96. The pharmaceutical composition of claim 94, wherein the TNF-related ligand is TRAIL.